

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

CLAIMS

1. A humanized antibody or an antigen-binding humanized antibody fragment, wherein said antibody or said antibody fragment binds specifically to the antigen bound by antibody NR-LU-13.

2. A humanized antibody or an antigen-binding humanized antibody fragment according to claim 1, wherein said antibody or said antibody fragment specifically binds to the antigen bound by antibody NR-LU-13 and wherein said antibody or said antibody fragment either does not possess N-linked glycosylation or its N-linked glycosylation has been modified post expression to reduce immunogenicity or toxicity.

3. A humanized antibody or antibody fragment according to claim 2 wherein said antibody or said antibody fragment does not possess N-linked glycosylation.

4. A humanized antibody or antibody fragment according to any one of claims 1, 2 or 3 wherein said antibody or said antibody fragment has been mutated to prevent N-linked glycosylation.

5. A humanized antibody or antibody fragment according to claim 2 wherein the N-linked glycosylation of said antibody or said antibody fragment has been modified post expression to reduce immunogenicity or toxicity.

6. A humanized antibody or antibody fragment according to claim 5 wherein the N-linked glycosylation has been modified chemically.

7. A humanized antibody or antibody fragment according to claim 6 wherein the N-linked glycosylation has been modified by oxidation.

8. A humanized antibody or antibody fragment according to claim 7 wherein the N-linked glycosylation has been modified by oxidation followed by stabilization of the aldehydes generated by oxidation.

9. A humanized antibody or antibody fragment according to claim 8 wherein the N-linked glycosylation has been modified by oxidation followed by reduction.

10. A humanized antibody or antibody fragment according to any one of claims 1-9 wherein O-linked glycosylation of said antibody or said antibody fragment has been reduced or eliminated.

11. A method of reducing immunogenicity or toxicity of an antibody or an antigen-binding antibody fragment of IgG class, comprising the steps of:

- (a) selecting a host system for the characteristic that said system does not N-link glycosylate an antibody or an antibody fragment; and
- (b) expressing in said host system a nucleotide sequence comprising nucleic acids encoding an IgG antibody or an antigen-binding antibody fragment.

12. A method of eliminating N-linked glycosylation in an antibody or an antigen-binding antibody fragment of IgG class to reduce immunogenicity or toxicity, comprising expressing in a host system a nucleotide sequence comprising nucleic acids encoding an IgG antibody or an antigen-binding antibody fragment, wherein said host system does not N-link glycosylate said antibody or said antibody fragment.

13. The method of claim 11 or 12 wherein said host system additionally does not O-link glycosylate the antibody or the antibody fragment.

14. The method of claim 11 or 12 wherein said nucleic acids encode a humanized antibody or antibody fragment.

15. The method of claim 14 wherein said humanized antibody or antibody fragment binds specifically to the antigen bound by antibody NR-LU-13.

16. The method of any one of claims 11, 12, 13, 14 or 15 wherein said nucleic acids have been mutated to prevent N-linked glycosylation.

17. The method of any one of claims 11, 12, 13, 14, 15 or 16 wherein said host system is a plant host system.

18. The method of claim 17 wherein said plant host system is from corn.

19. A method of modifying the N-linked glycosylation of an antibody or an antigen-binding antibody fragment of IgG class, comprising subjecting said antibody or antibody fragment to a post expression modification that modifies the N-linked glycosylation.

20. The method of claim 19 wherein the N-linked glycosylation is modified chemically.

21. The method of claim 20 wherein the N-linked glycosylation is modified by oxidation.

22. The method of claim 21 wherein the N-linked glycosylation is modified by oxidation followed by stabilization of the aldehydes generated by oxidation.

23. The method of claim 22 wherein the N-linked glycosylation is modified by oxidation followed by reduction.

24. The method of claim 23 wherein said oxidation is with NaIO_4 and said reduction is with NaBH_4 .

25. The method of any one of claims 19, 20, 21, 22, 23 or 24 wherein said antibody or said antibody fragment is humanized.

26. The method of claim 25 wherein said humanized antibody or antibody fragment binds specifically to the antigen bound by antibody NR-LU-13.

27. An antibody or antigen-binding antibody fragment of IgG class produced by the method of any one of claims 11-26.

28. An antibody or an antigen-binding antibody fragment of IgG class produced by the method of any one of claims 17, 21 or 22.

29. The antibody or antibody fragment of claim 27 or 28 wherein said antibody or said antibody fragment is humanized.

30. The antibody or antibody fragment of claim 29 wherein said humanized antibody or antibody fragment binds specifically to the antigen bound by antibody NR-LU-13.

31. A conjugate comprising a humanized antibody or antibody fragment according to any one of claims 1-10 attached directly or indirectly to a ligand or anti-ligand.

32. A conjugate comprising a humanized antibody or antibody fragment according to any one of claims 1-10 attached directly or indirectly to a diagnostic agent.

33. A conjugate comprising a humanized antibody or antibody fragment according to any one of claims 1-10 attached directly or indirectly to a therapeutic agent.

34. The conjugate of any one of claims 31, 32 or 33 wherein said antibody or antibody fragment is prepared according to the method of any one of claims 11-18.

35. The conjugate of any one of claims 31, 32 or 33 wherein said antibody or antibody fragment is prepared according to the method of any one of claims 19-26.

36. The conjugate of any one of claims 31, 32 or 33 wherein said antibody or antibody fragment has been expressed in insect cells, mammalian cells, bacterial cells, yeast or plant cells, or has been modified by oxidation followed by reduction, or has been mutated to prevent N-linked glycosylation, or combination thereof.

37. The conjugate of any one of claims 31, 34, 35 or 36 wherein said ligand or anti-ligand is biotin, avidin or streptavidin.

38. The conjugate of claim 37 wherein said ligand or anti-ligand is streptavidin and wherein said antibody is NRX451 or said antibody fragment is derived from NRX451.

39. An antibody or antibody fragment or method or conjugate according to any one of claims 1-38 wherein said antibody or said antibody fragment specifically binds to the same epitope as antibody NR-LU-13.

40. An antibody or antibody fragment or method or conjugate according to any one of claims 1-38 wherein said antibody is NRX451 or said antibody fragment is derived from NRX451.

41. The humanized antibody NRX451 or an antigen-binding fragment thereof.

42. The antibody or antibody fragment of claim 41 wherein said antibody or said antibody fragment either does not possess N-linked glycosylation or its N-linked glycosylation has been modified post expression to reduce immunogenicity or toxicity, and

wherein said antibody or antibody fragment specifically binds to the antigen bound by antibody NR-LU-13.

43. The antibody or antibody fragment of claim 42 wherein the N-linked glycosylation has been modified chemically.

44. The antibody or antibody fragment of claim 43 wherein the N-linked glycosylation has been modified by oxidation followed by stabilization of the aldehydes generated by oxidation.

45. The antibody or antibody fragment of claim 44 wherein the N-linked glycosylation has been modified by oxidation followed by reduction.

46. The antibody or antibody fragment of any one of claims 41-45 wherein said antibody or said antibody fragment has been mutated to prevent N-linked glycosylation.

47. A pharmaceutical composition comprising an antibody or antibody fragment or conjugate according to any one of claims 1-10 or 27-46 in combination with a pharmaceutically acceptable carrier or diluent.

48. An antibody or antibody fragment or conjugate or composition according to any one of claims 1-10 or 27-46 for use as a diagnostic or as a medicament.

49. The antibody or antibody fragment or conjugate or composition of claim 45 for use in diagnostic or therapeutic pretargeting methods.

50. Use of an antibody or antibody fragment or conjugate or composition according to any one of claims 1-10 or 27-46 for the manufacture of a diagnostic for the diagnosis of cancer, or of a medicament for the treatment of cancer.